The specification has been corrected by referring to sequences by Sequence I.D. Nos.

The reference to the U.S. Patent Application is retained as it is in the Background of the Invention. The restriction to incorporation by reference referred to by the Examiner does not apply to background art. Patent Applications referred to in patents are obtainable from the U.S.P.T.O (MPEP 608.01p).

Claims 1 - 11 and 15 have been rejected under 35 USC 112 as being indefinite in that they only describe the compositions by arbitrary laboratory designation.

This objection has been overcome by amendment since the compositions have now been defined by structure and function.

Claims 2 and 7 have been rejected on the ground that the meaning of "a portion" cannot be determined.

Claims 2 and 7 have been cancelled.

Claims 1 - 11 and 15 have been rejected under 35 USC 112 on the ground that the specification is not enabling for the claims as broadly presented.

The specification must be read within the environment of known art.

One skilled in the art can easily obtain an active p53, simply by truncating it or otherwise modifying its carboxy terminal end to destroy its negative regulatory domain. This is easily done and easily tested as described in Hupp, et al. (1992) "Regulation of the specific DNA binding function of p53" Cell 71, 875-886, of record.

Unfortunately, destruction of the regulatory domain, without more, leaves a serious problem and that is that there is no easy and practical way to distinguish between normal p53

and the activated p53 because there is no clearly distinguishing epitope which gives rise to an antibody which will react with the activated p53 but not with normal p53.

A natural p53as was discovered by the present inventor which both lacked these negative regulatory domains of p53 and had an epitope unique to p53as which could give rise to an antibody reactive with the p53as but not p53.

It was then further discovered that any activated form of p53, as taught by Hupp, et al., could be made into a p53as as described in the present invention by adding or creating a unique epitope at its carboxy terminal end. The teaching is the specification of the creation of such an epitope giving rise to the unique ApAs antibody enables one skilled in the art to easily incorporate others. The result is that the p53as is active in cellular environments where p53 is not and has a unique epitope not present in p53. The unique epitope depending upon its selection, permits the carboxy terminal end of the p53as to be longer or shorter than normal p53 which, in fact, permits p53as itself to be longer or shorter than the corresponding p53. One skilled in the art can easily determine where p53 has been truncated too much so that it no longer acts like active p53 or when the added or created epitope is so long that it interferes with activity. Thus, there are many possible p53as's against which unique antibodies may be readily made by the teachings of the specification.

There is more than ample teaching to enable making the p53as materials described in the specification as well as antibodies thereto.

Furthermore, in accordance with the present invention, one skilled in the art is clearly enabled to incorporate a cDNA sequence into a plasmid or viral vector which encodes a p53as as described.

There is no ambiguity and no lack of enablement.

The rejections of the claims based upon lack of enablement should be withdrawn.

Claims 1 - 4 have been rejected under 35 USC 102 as being anticipated by Wolf, et al.

There is no disclosure or suggestion in Wolf, et al. that the cDNA of Wolf, et al. encodes an alternatively spliced p53 which is active in cellular environments in which p53 is deactivated due to its negative regulatory sequence. Nor is there any disclosure or suggestion in Wolf, et al. that the cDNA of Wolf, et al. encodes an active alternatively spliced p53 having a unique epitope which gives rise to an antibody which will recognize the alternatively spliced p53 and not p53.

The rejection based upon Wolf, et al. is improper and should be withdrawn.

Claims 1 - 4 and 15 have been rejected under 35 USC 102(b) as being anticipated by Han, et al. Han, et al. does not anticipate these claims and does not suggest them. This Han, et al. rejection is based upon classic hindsight.

Han, et al. used cDNA for analysis but did not incorporate it into a vector. Han, et al. is concerned with p53 RNA and with respect to AS-p53RNA says "AS-p53RNA species are predicted to result in premature termination of p53 protein, making it 9 amino acids shorter and differing in 25 amino acids at the C-terminus."

Han, et al. is concerned with p53 RNA and does not even teach that a p53as protein exists, but suggests that if it did exist, its terminal sequence might be different that p53. There is no suggestion that such a speculated protein might contain a unique epitope sequence not present in p53. A difference in a terminal end might simply mean a shortening which would mean the speculated protein contains no sequences which are not also present in p53. It is a giant unsupported step in hindsight to say it is obvious that a specific antibody can be made to a protein whose existence is not certain and whose structure is speculative. Further no nucleic acid sequence encoding a p53as in accordance with the invention is incorporated by Han, et al. into a plasmid or viral vector.

This is hardly a teaching that can be relied upon in view of the fact that the Examiner has taken the position that even the detailed teachings of the present patent application are insufficient. Neither position of the Examiner is correct. The detailed teachings of the present application are sufficient under 35 USC 112 and the speculative suggestions of Han, et al. are not sufficient under 35 USC 102 or 35 USC 103, whether or not Han, et al. is combined with other cited references.

Claims 1 - 4 and 15 have been rejected under 35 USC 102 as being anticipated by Arai, et al.

Arai, et al. does not anticipate or suggest the present invention. The Arai, et al. reference suggests that an alternatively spliced p53 (p53-M8) can be made which is 9 base pairs shorter than p53. Arai, et al. also says that p53-M8 is in other respects identical to p53 except that p53-M8 was lacking the pAb421 - pAb122 antibody site.

There is no suggestion or teaching whatsoever that the Arai, et al. p53-M8 lacks the negative regulatory domain of p53 or that it has a unique antibody site not present in p53.

Claims 5 - 11 have been rejected under 35 USC 103 as being unpatentable over Wolf, et al., Han, et al., or Arai, et al. in view of Lee, et al.

This rejection is improper and should be withdrawn. Wolf, et al., Han, et al., and Arai, et al. are defective references for reasons previously given. In particular, none of them or their combination suggest an alternatively spliced p53 having a unique epitope not present in p53 and lacking the C-terminus negative regulatory domain of p53, nor a cDNA sequence encoding such an alternatively spliced p53, nor a plasmid or viral vector containing such a cDNA sequence, all of which are required by the present claims.

Lee, et al. does not correct these critical defects.

Lee, et al. comprises a somewhat generic disclosure for producing polypeptides in insect cells using cDNA in viral vectors. Lee, et al. suggests nothing concerning any p53 structure and therefore can not correct the defects of Wolf, et al., Han, et al., and/or Arai, et al.

Further, such a combination is based upon impermissible hindsight since none of Wolf, et al., Han, et al. nor Arai, et al. suggest any reason to place any of their nucleic acid sequences into a virus.

It is requested that the requirement for formal drawings be delayed until there is an indication of allowable subject matter.

All rejections should be withdrawn and all claims should be allowed which action is courteously requested.

Respectfully submitted,

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